The following written statements were sent in prior to the meeting to be presented at the meeting:

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" **Jehn, Donald**

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From: Lynn Amer'
Sent: Sunday, September 18. 2005 9:01 PM
To: donald.jehn@fda.hhs.gov
Subject: Approve Exjade

Blood Products Advisory Committee,

I recently learned that you are reviewing the New Drug Application for the oral chelator Exjade (ICL670). I would I to encourage you to approve Exjade for use in the US. Europe and Canada approved the use of oral chelators years ago. My friend suffers from Thalassemia. The pain and inconvenience caused by the Desferal injec~ons is unreasonable for her to have to endure when an alternative is available. I have heard her say that she does not administer her injections at times in her life because it is too painful and difficult to do. "She says she would absolut~ use the oral chelator if it was available. Please approve the use of Ex jade in the US in order to save the lives of my friend and the many others who suffer from lack of a reasonable treatment of their chronic iron overload due to the transfusions they undergo.

Sincerely,
Lynn Arner-Cross,

. -

9/19/2005

. .' Jehn, **Donald**

From:
Sent: Sunday, September 18. 2005 6:35AM
To: donald.jehn@fda.hhs.gov
Cc: ~....
Subject: The Urgent need for an oral alternative for Desferal

Donald W. Jehn
Center for Biologics Evaluation and Research (HFM-71)
Food and Drug Administration
1401 Rockville Pike
Rockville, MD 20852
301-827-0314

Subject: The Urgent need for an oral alternative for Desferal

Dear Sir,

No one can imagine how painfuL annoying and stressful the Daily Desferal therapy for Thallasaemia patient is. b the patient who try hardly to survive and in order he give up a. lot of things that normal people do in their daily rutine.., he give up his freedom for more than 8 hours by using Desferal. which limits his or her relations and activities..
I am a 37 years old Thallasemia Major patient and I've been taking Desferal for more than 24 years...almost on d basis.
When Desferal was the only chance to survive the iron overload complications. we 'couldn't really imagine our fu with being trapped home attached to the pump for more than 8 hours a day... which made traveling. having relationships almost impossible! !.

Many talented patients couldn't even complete their education or capture a good job opportunities because of this regime.....
As we get older more complications get oUr attention. but taking Desferal Su~ Q remains our big complications. our skin start getting rough. and we run out of spots.. .and so many patients give up the chelating therapy because the compIlcation of taking Desferal by subQ.

.In a social study. I made few years ago with co-operation with Thallasemia International Federation(TIF-Cyprus] found out that not less than 25% the patients (specially from age 30-45) stop taking their Desferal because of Irritation, allergy. rough skin or getting problems while infusing Desferal or for other social and Psychological
reasons.

Unfortunate'}y from Age 22-29 I found that 45% patients stop or reduce and minimize their Desferal Intake becal of their style oflife as teenagers..! !
Many patients don't mind to follow up more often with their clinics or hospitals. if that will provide them with gc alternative for Desferal, and that was the reason I participated with Dr. Robert Grady. and Dr. Patricia Giardina (York Hospital) more than 7 times each time was for 34 days to try the Oral therapy within a protocol (human tria

Having alternative oral therapy is our great hope. and is our only chance to survive before we give up. it will mal
our lives easier and will. help us to get red of the stored iron and cleanup our cells and organs before we start fal apart.... .
Thank you for considering reviewing the oral chelator Exjade (ICL670). We appreciate this chance...

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I do really appreciate your time mid consideration
God Bless You..

Ned

Houston- TX 77042
Tel:.
Fax:

East West Newspaper .Sharq Garb
P. O. *Box 571902, Houston, TX* 77257, *USA*
www.sharqgarb.com

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9/19/2005

Jehn. Donald

~ r; lJ P c, "fC,

From: Alfred
Sent: Sunday, SeptEtmber 18, 2005 2:57 AM
To: donald.jehn@fda.hhs.gov
Cc:
Subject: Oral Chealator

Dear Dr. Donald .;rehn:

I am a parent of a 18 year old son who has beta thalassemia major. He has been transfusion dependent since he was six months old. 1 started chelation therapy when he was two years old and it was a nightmare. His veins kept collapsing and during one transfusion he had to endure 12 IV's the last one in "his neck. The needle broke and he was not able to receive the proper amount of blood. Imagine the aversion he had with injectable desferral. The treatment was painful, unpleasant, and forced him to be shackled to a pump. We eventually had a port a cath inserted in his chest in the hopes it would alleviate his transfusion and chelation treatments. It made life easier for all of us for nearly a year. Then the port broke through his chest and he had to have *it* removed. We tried two more ports and lost one through infection while the other port clogged and had to be removed. The fact was that there was no easy way at that time to get iron out of his body.

When 1 was born I spent a lot of time researching the effects and problems associated with my son's condition. We "had high hopes that a cure would be found. At the very least I heard that the oral chelator would become a reality and improve the patients compliance with chelation therapy. Non complia~ce meant death! I attended a variety of conferences, medical seminars, etc searching for answers. We have waited 18 years and many patients have died in that time span. I emphatically urge you and the committee to approve the use of the oral chelator ICL670. We have waited long enough lets give these patients the relief they deserve.

Sincerely, Alfred

- Jehn, **Donald**

~CiJ~CTf.

From:
Sent: Friday, September 16,20057:53 PM
To:" donald.jehn@fda.hhs.gov
Subject: Exjade-oral chelator

Dear Mr. Jehn.

I am writing regarding the Blood Products Advisorv Committee's pending review of the New Drug Application for the oral chel
Exjade (ICL670) on September 29. My wife, - " has thalassemia, and despite the fad that she uses Desferal mo
regularly and rigorously than any other person with thalassemia that I know, she could clearly use an oral chelator such as Ex
When my wife takes her infusion of Desferal, she must puncture the skin of her legs or stomach with a needle to insert her po She often does this every day for weeks at a time before giving herself a break of a day or two. She needs these breaks to le' bruises heal where she inserts her needles. day in and day out She is committed to doing her Desferal as much as possible.
. .because she. is happily married and wants to extend our life together as long as s~ .can. How much nicer would it be for her could take her break every so often and take an oral chelator during those days! Her bruises could have more time to heal. bl she would still be removing iron from her body by using the oral chelator. Her quality of life is already high-despite the fact tl she must make hospital visits every three weeks for blood transfusions and take a host of oral medications-because she ta~ VERY good care of herself. How much higher would it be if she could use an oral chelator a few times a month?

We know many people with thalassemia who are not as compliant with their Desferal regimens as ; Unlike my dear wi some of these people cannot handle the idea of sticking themselves with a needle every day. even if it means extending theil lives. Approval of an oral chelator could help these people immensely. I am sure that if you were forced to stick yourself with needle every day. you, too, would be very eager for anything that would enable you to do it Jess! We also know people with thalassemia and diabetes who must stick themselves multiple times a day to test their blood sugar. Wouldn't it be much nicer them if they could avoid one more needle-stick per day in a life that is full o~ .sharps? .

On behalf of my wife, as well as other patients with thalassemia. I ask the FDA to please approve the use of Exjade. It is disgraceful that oral chelators have been available in Europe and Canada for years, but they have not been approved in the United States. How can. members of our medical community assert that they are part of the most technologically and medica advanced nation in the world when treatment for thalassemia is so much farther along in other countries? The approval of E)I could help remedy this and aid in raising the quality of life for all thalassemics in the United States.

Thank you for .taking the time to read my note.

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Jehn, Donald

t? (;/)Ac rt:1.

From: #.

Sent: Friday, September 16, 20054:08 PM

To: donald.jehn@fda.hhs.goY

Subject: Exjade Approval- Sept. 29, 2005

My name is .. -- , .1 am a 35 year old with beta Thalassemia. I have been transfusion dependen1 since an infant. As a result iron over load has been a major health concern. Since age seven I have rea the benefits of a highly effective subcutaneous iron chelator named Desferoximine (aka Desferal). I acti1 participated in all phases of the FDA trial studies for this agent in the mid 1970's. Similarly, I am currentl participating in the final trial studies for an oral iron chelator called Exjade (aka ICL670). On. September 29th, 2005 The Blood Products Advisory Committee will review the new drug application for Exjade. The committee will then make a recommendation to the FDA as to whether to approve Exjade for use in the United States. I am writing this email to you as my own personal testament in support of Exjade's appro

0-. The only available option I have for iron chelation therapy is the subcutaneous infusion of the drug DesfE I began using Desferal in 1977. For the past 23 years I insert a needle under my skin and slowly infuse. drug over an 8 eight period of time with a battery operated pump. It is a tedious and extremely painful regiment that requires an exorbitant amount of effort and determination in order to maintain compliance.

Because I am compliant I have reaped the rewards of this wonderful and effective drug. I live my life witt Th~h:lssemia more as a mere inconvenience rather than an unbearable burden. I have a college educat I enjoy both a fulfilling and successful profession, I have beautiful a wife that willingly stands by my side, .. .is proud to say that I am her husband, two amazing loving daughters that I adore with all my heart and a family that serves as- an uplifting source of support and believes in my abilities as a man and a father.

In. most instances things get easier over time. I. can personally attest that this is not the case with subcutaneous iron chelation therapy. The pain and compliCations you endure from subcutaneous chela1 therapy worsen each day and maintaining a consistent level of compliance grows harder and harder. BE complaint was an "easier task" (for the lack of better words) when I was younger and the only life I was responsible for was my own. Fortunately, that is no longer my case and I have a lot more to live for.

For the past 18 months I have taken Exjade for investigational purposes. Exjade has provided me with; quality of life that I have only dreamed about and have never experienced. Most importantly Exjade has given me hope and has provided me with renewed confidence in being compliant with my iron chelation therapy and my overall health.

It is imperative that Exjade wins approval on September 29th, 2005. The patients of Thalassemia must an alternate treatment of iron chelation therapy that offers an improved quality of life. Thalassemia patie have made many sacrifices over the years and have waited a long time for an oral chelator such as Exja to come to fruition. Time is running out and this must be approved.

Thank you for your time and consideration.

Sincerely,

Freehold, NJ 07728

9/19/2005

Jehn, Donald

R~Act"('D

From:
Sent: Monday, September 19,200511:26 AM
To: donald.jehn@fda.hhs.gov
Subject: Check out About Thalassemia

About Thalassemia

Our son has been using iron chelation therapy for nearty 30 years. Although this has helped control the iron overload causet

the transfusion of washed and packed red cells over the last 25 years, the ever present danger of Bacterial infection from tl . medi-port installed in his main artery to his heart, shows the need for an Oral Chelation pill to replace the need for the Med port. We hope that FDA Makes the pill available in the United States to our son and other Thalassemia Major patients. This would also benefit Sickle cell anemia patients who get transfusions to have a chance of leading a better life. .'

Thank

you Mr. & Mrs.

J(

Jehn, Donald

pGfJAci(O

FrOm: - - . 0 ------- ,
Sent: Wednesday, September 21, 2005 2:20 AM
To: donald.jehn@fda.hhs.gov
Subject: Iron Chelation! thalassemia

Dear
Sir,
Actually; my daugther is tthalassemia patient, .

my daguther details as
under;
1. Patient Name. : - -r- --.
2. Date of Birth: 20th May 1996 (10 Yrs)
3. Blood transfusion: Every month 2 bottle
4. currently using of Iron chelation: Keifer 500mg capsule (Cipla'Company)
5. Feertin .0 1804
6. Suggestion: any progress of thalassemia treatement
70 ICL670 medicine avilable in India - 0 0
8. my personal Address: - - 0 -'~..... ..V.- .-, - - - n ... "...,
-.
-- -
. - India

M)'- finanical background is poor. I am working in pvt. company.

Please reply to me.

Thanking you

Yours Truly, - .
D

MS., CRNA., ARNP

R €-
&Tt0

September 21, 2005

Donald \v. Jehn .
Center for Bioiogics Evaluation and Resean:h
Food and Drug AdministDtion
1401 Roc:kviJle Pike
RockviJ1e, MD 20852

Dear Mr. Jehn:

This letter is in reference to pending approval of the ORAL iron che1a1ing drug, Exjade (lCL 670)~ I hope that you sincerely consider its approval as an alternative to subcutaneous, and intravenous infusions of Desferal.

I am a 33 year old Thalassemia ~Iajor patient that has received painful subcutaneous and tedious intravenous infusions of Desferal to maintain a normal ferritin level throughout my life. ..\s a chronic recipient of blood transfusions, this treatment is mandatory for me to survive. Although Desferal has been a lifesaver, Exjade could prove to be a drastic improvement in my quality of life, as it will in many other patients' lives. BlOOd transfusion dependency is burden enough, but infusions of Desfenl every day creates a burden that nobody could understand. To simply consume an oral iron chelator would be a fantasy that I can only imagine.

The global clinical trials of Exjade have demonstrated that this drug is equal, if not superior in reducing liver iron stores. This could also mean higher compliance in Thalassemia patients, which would lead to a longer life expectancy. The main reason for the failure of Desferal is the non-compliance related to the painful injections and burdensome treatment.

11y professional life consists of full rime employment as a Certified Registered Nurse _-\nesthetist. In this capacity, my rime is also spent receiving blood transfusions every three weeks along with the infusion of
. Desferal five days per week via an intravenous catheter implanted under my. skin and into my subcla.vian vein. When I am at work administering anesthesia. I must also receive this intravenous medication and/ hope that nothing goes wrong while it is infusing into my body. Not only is much of my rime consl.~..d by administering my medication, but I am also at risk for lethal septic infections. and failed ports. These ports can also clot, and become worn our over a penod of time. There is also a risk for pump malfuncnons. which can also prevent infusion of the medicatJon. This IS reason enough for the appro,'al of a less invasi"e. quality tmpro"mg ORAL iron chelator.

I think I speak for all Thalassemia patients. health professIonals. and those afflicted with hemachromatosls when I state that a safe and effective oral iron chelator such as EXlade IS ver\' long overdue.

Sincerely,

Thalassemia ~lajor Patient.

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"liON

Jehn, Donald *~f5/JlJrtc*

From: - --r-- _. -.
Sent: Tuesday, August 30, ;lU05 5:50 **PM**
To: donald.jehn@fda.hhs.goY
Subject: Exjade Approval- My daughter Major Jhalassemia

Hi Donald W. Jehn,

This *is* - . *l* (Pakistani) National working in Saudi Arabia, actually I camto know through net about Exjade Approval in process.

My daughter four years old *is* the patient of Major Thalassemia getting blood transfusion every month and since a year or so we started the chelation therapy of Desferal due to high Iron Overload.

Now weare puttin9 our eyes for Oral Desferal approval *like* Exjade which can help my daughter to decrease her Iron and in addition to that get *rid* of the pain of getting chelation therapy over the night.

So please keep me in your mailing list for the update going on for Exjade Approval.

Thanks for your cooperation...

Regards,

Saudi ..Arabia
Tel: . - . -

Jehn, Donald.

From: Robert Grady
Sent: Friday, September 23, 2005 3:52 PM
To: Donald Jehn
Subject: Blood Products Advisory Committe

Dear Dr. Jehn,

I ~nadvertently used the wrong e-mail address (hss, Hospital for Special Surgery, right next door) in sending you information yesterday. Below *is* the intended information. While I realize that it *is* now late, I ask that you take it into consideration in your deliberations.

Dear Dr. Jehn,

I will be attending the meeting of the Blood Products Advisory Committee on September 29, 2005 and would like to make the following comment~.

Exjade (ICL670) will be a useful iron-chelating drug and should be made available to patients.

On the other hand, it is not a suitable replacement for Desferal (desferrioxamine) in many patients. The most recent approach has been to demonstrate that Exjade is non-inferior to Desferal. While many parameters could and should be compared, the emphasis has been on iron excretion/iron balance. Direct comparisons of iron balance in the same patient have not been carried out. Instead, historical ranges or surrogate parameters have been utilized. This could be misleading given the wide patient to patient variability that has been demonstrated in both Desferal- and Exjade-induced iron excretion~ Ln the largest trial of Exjade conducted to date, changes in liver iron concentration and serum ferritin over the course of 52 weeks were used as surrogate markers of iron excretion/iron balance. In both groups, those getting Exjade and those infused with Desferal, a significant number of patients failed to achieve negative balance even at the highest doses tested. Simply comparing mean values doesn't prove the non-inferiority of Exjade *in* comparison with Desferal. Were the changes *in,* liver iron concentration and serum ferritin in a given patient consistent /~ with respect to the assessment of iron balance? Did the relative changes in these parameters accurately reflect the differences in the trans£u~ic~ regimens (iron input) of the patients? And to which combination of doses is the terminology non-inferior being applied? In most pat~ents, 10 mgikg of Exjade would be inferior to 40 mg/kg of Desferal. Even 40 mg/kg Exjade is not capable of putting all patients into negative iron balance. Nor is 40 mg/kg of Desferal for that matter. It should be determined in what percentage of patients the effectiveness of Exjade is actually better than, equal to or less than that of Desferal if non-inferiority is to be established. This cannot be done by comparing group means of surrogate markers, where the response to each of the individual drugs is not known. It *is* likely that some patients respond very well to Exjade but less well to Desferal and vice versa. Transfusion requirements must be taken into account.

It will be good to have Exjadeas another option for the patients. It *is* unlikely that any drug will be useful throughout the life of a given patient. As changes in lifestyle occur, different regimens will probably be needed. Undoubtedly, combinations of drugs will prove to be the most effective approach. Exjade should be approved on *its* own merits without taking away from Desferal. Apart from its mode of administration, the latter *is* a superior drug which has markedly improved the lives of many patients suffering from iron overload.

Sincerely,

Robert W. Grady, Ph.D.
Associate Research Professor

Tel: Fax: e-mail:

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To the Blood 'Products Advisory Committee:

I am a patient diagnosed with Thalassemia (aka Cooley's Anemia) Beta Major since birth. I am currently 28 yrs old and reside in RockVille, MD and have so my entire life with the exception of going off to college.

As a Thal,patient; I can inform you that current treatments require patients to inject themselves subcutaneously several times a week. I have to inject myself for 5 nights a week. The injections help reduce the iron level in my body which is detrimental to my organs and other parts of my body. The iron overload is a result of me being transfusion dependant. The constant blood trans~ion that I have received over the last 20 yrs have caused for a high level of iron to exist in my body.

I personally have been very compliant with,my treatments and have regular visits with numerous doctors to make sure I maintain a status quo in terms of iron level. hemoglobin. growth development, as well other as other test to make sure that organs normally impacted by the iron are remaining as healthy ~ possible. Some of the test d°l.le are bone age (x-rays), blood test drawn, ECHOs, EKGs, Hearing and Vision tests, T2* (heart test). Squid test (liver). MRIs, and a slew of others. I have been very fortunate to have parents who have had very good jobs that have supplied the best medical care. I have also ~n very fortunate to have been very well educated at James Madison University and been able to be employed by Fortune 500 companies who provide very good health care plans. Other patients are not as fortunate since ThaI prevents them from being able to work full time. Some effects of ThaI is that you always feel tired and hot. At times you just can not keep up with a lot of physical activity due to the lack of oxygen binding to the hemoglobin. I feel this especially when I am at the week before] 'am due for my , "transfusions.

Since I have been diagnosed with Thalassemia at birth this is all I know so the sense of "normalcy" for me is there. However patients who have not always liveti like this can run into problems of being very rigid in their treatments. 'Many patients become non compliant or have a hard time adjusting to life with all the doctor's appointments and treatments. Not being compliant with desferal can cause other complications such as diabetes, heart and liver malfunctions, other organs malfunctioning. and reproductive issues as well t~,name a few. While all patients should remain'compliant. it can be very, " difficult to deal with every day life from trying to balance a family. work. social life. and treatments. For younger patients the results of the treatments may not seem so 'evident' because it takes a while for the high concentration of iron to take effect. But when it does, the patient is in tremendous pain albeit brought on by their non-compliancy.

I am a new proud parent of a healthy 4 month old son. Due to my genetic disease he is now a carrier of Thalassemia and will pass this trait down to my grandchildren. Fortunately, with medical advances today. I have stored his cord stem cells with a stem cell bank in hopes that future studies will show how to cure this disease. In years to come will become aware of what his daddy has to go through in terms of being compliant with my medicatien'and numerous test and doctor's visits I must go through. I will

eventually have to make him aware ofThal and'how it may impact his life and that of his children.

I am pleading with the "Board" to please approve-tbe Novartis Pharmaceuticals' New Drug Application (NDA) for Exjade (deferasirox), formerly known as ICL67. Not only will it make. an impact close to home but to others world wide. The comfort of not. . having to' deal with the pain of injecting yourself on a nightly ritual is something I have been longing for and look forward to. I pray and hope that in the near future this is something that can come true. Thank you *for* your time.

Sincerely

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. .' Rockville, MD 20850

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CIICAGDIe !GSB

R6Jj/lCTI:O

The Universi~' of Chira~o
Graduate School of Business
5807 South Woodlawn Avenue
Chicago. Illinois 6063:
Tel
Fax' .

September 11, 2005

Dr. Donald W. Jehn
Center for Biologics Evaluation and Research (HFM-:
71)
Food and Drug Administration
1401 Rockville Pike'
Rockville, MD 20852

Dear Dr. Jehn:

New Drul!-ADpiication eNTIA) 21-882 nrooosed trade nanie EXJADE
ldeferasirox) Tablets for Oral SUSDension. Novartis Phannaceutical Com.

I have a six-year old son, named. - who was born to my wife and me after 11 years of marriage, three miscarriages and several years of infertility treatment. Unfortunately, - "suffers from a blood disorder called beta-thalassemia, and needs chrOnic red cell transfusions every few months. While he currently remains healthy and his iron levels are controlled by IV desferal administration, my wife and I pray every day for the approval of the oral iron chelator, EXJADE.

As parents, we want our son to ,continue to be healthy and not have iron overload because of his chronic transfusions, but fear that the current standard of treatment, subcutaneous or IV administration of desferal, is too painful for a little boy to go through. Were I;te'not to comply with this painful procedure, either now or especially when he grows up to be a teenager (when he will probably want to make his own decisions), we do not want his life to be at risk, as we have seen happen to several teenage betathalassemia patients. Finally, it seems like we have a safe and efficacious orai iron chelator, that might provide a more humane option for iron ch~at:~n to little children like - , to lead a better quality oflife yet remain healthy. Therefore, as a father, I implore the FDA to approve EXJADE, to provide families like mine a little relief from the pain, suffering and mental anguish that accompanies us dealing everyday with this chronic illness, and let my little son lead a better quality of life yet remain healthy.

I will remain forever indebted for helping my son,

Sincerely,

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Chicago,
IL 60637
Tel: .

September 11, 2005

Dr. Donald W. Jebn
Center for Biologics Evaluation and Research (HFM-71)
Food and Drug Administration
140 1 Rockville Pike
Rockville, MD 20852

Dear Dr. Jebn:

New Drug Application (NI)~2 prooosed..!mde name ~E "ldeferasirox)
Tablets for Oral Susoension. Novartis Pharmaceutical Com.

I am the mother of a six year old boy named who suffers from Thalassemia. His condition requires him to take red cell transfusions regularly. My husband and I were able to conceive. . l after many years of infertility treatments, miscarriages and an ectopic pregnancy. When *I* - was finally bom,he was our biggest dr~~ come true. We have worked very hard and have made it our mission to keep him as healthy as possible and give him the best quality of life that he so deserves. 1 'u has had a single donor from whom he receives his red cell transfusions. I have given up my career and all other pursuits in order to focus as much as I can on his diet and every other avenue that can contribute towards improving his health for the future. I have been. through many IVF cycles and am still trying with the help of Pre-Implantation Diagnostics to see if our third. child could be a match fOI. . . so he can benefit from stem cell transplantation.

.My husband and I have attended many conferences and met with families who ha~

children suffering from the same genetic condiilon. The main concern of all parents is the risk of iron overload (which is the leading cause of fatalities) and the problem of compliance among children, with the established method of iron cnelation. My son is extremely positive and enthusiastic about life, despite the number of times he has to visit. . the hospital, get tested and examined, and undergo the sometimes painful transfusions. I fear to think what impact tht.: regular pumping of medicines will have on his spirit and more so what if he does not want to comply?

I implore you as the mother of a little boy (and on behalf of all the other kids with this chronic condition) who is just starting out to discover the joys of living, to approve the oral iron chelator, EXJADE. It will have the greatest positive impact on his quality oflife and for us as his parents, we could ask for nothing more for our son.

I will remain forever indebted for helping my son, *j* .

Sincerely,